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Retinoic acid (RA) patterns embryonic vertebrate hearts in the anterior–posterior (AP) axis, dividing them into inflow/outflow segments (e.g., atrial or ventricular chambers). RA patterning extends to teleosts, suggesting that hearts are composites of inflow/outflow segments presaged by division of precursors along embryonic axes by signaling mechanisms. We argue that chambers arose in evolution, not one by one, but simultaneously, as an ancestral peristaltic pump field was patterned into domains later fashioned into chambers. We propose to use RA signaling as a tool to understand the origin of chambered hearts from the peristaltic vessels of deuterostomes. We and others showed that retinaldehyde dehydrogenases (ALDH1 and ALDH8) and RA receptors (RAR) are present in non-chordate deuterostomes, demonstrating that rather than being a chordate novelty, RA signaling was already present in the deuterostome ancestor. Work in invertebrate chordates indicates that tunicates and cephalochordates display phylum-specific duplications of aldehyde dehydrogenases from sub-family 1 (ALDH1). Therefore, deeper analyses of sequence, structure, expression and activity may be necessary to identify the enzymes that are directly involved in RA synthesis and to establish the relationship between their expression patterns and the progenitors of invertebrate chordate pumping organs. Similar to vertebrates, retinaldehyde dehydrogenases mark the posterior border of the emerging invertebrate chordate pump field. This suggests scenarios in which this ancestral topology was initially exploited to establish posterior boundaries of pumping organs, but was later co-opted to AP patterning roles.

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Program/Abstract # 15
Transcriptional control of second heart field development
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The second heart field (SHF) is a recently discovered population of cardiac progenitor cells that reside anterior to the primary or first heart field (FHF). SHF cells from the pharyngeal mesoderm are progressively added to the linear heart tube, which is derived initially from the FHF, at the time of looping to form the outflow tract, right ventricle, ventricular septum, and portions of the left ventricle. The LIM-homeodomain transcription factor ISL1 is required for SHF development and functions at the top of a transcriptional cascade for the development of this lineage. Likewise, the MADS domain transcription factor MEF2C is required for right ventricle and outflow tract development. We have recently shown that mef2c is a direct transcriptional target of ISL1 via a novel SHF-specific enhancer, establishing a direct link between these two essential factors. We have continued our analyses of the mef2c SHF enhancer by defining the epigenetic mechanism through which ISL1 results in sustained activation of this enhancer in the right ventricle and outflow tract after Isl1 expression itself is extinguished. To understand the earliest steps in SHF progenitor specification, we have also identified a distal transcriptional enhancer from the Isl1 locus sufficient to direct expression to the SHF at early cardiac crescent stage and to the pharyngeal mesoderm at the linear heart tube stage. We have begun to define the transcription factor and signaling pathways upstream of this novel Isl1 enhancer, which show how Isl1 integrates multiple signaling pathways to control SHF progenitor specification.

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Program/Abstract # 16
Vessel and blood specification override cardiac specification in anterior mesoderm
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Organ progenitors arise within organ fields, embryonic territories that are larger than the regions required for organ formation. Little is known about the regulatory pathways that define organ field boundaries and thereby limit organ size. Here, we identify a mechanism for restricting heart size through confinement of the developmental potential of the heart field. Via fate mapping in zebrafish, we locate cardiac progenitors within hand2-expressing mesoderm and demonstrate that hand2 potentiates cardiac differentiation within this region. Beyond the rostral boundary of hand2 expression, we find progenitors of vessel and blood lineages. In embryos deficient in vessel and blood specification, rostral mesoderm undergoes a fate transformation and generates ectopic cardiomyocytes. Therefore, induction of vessel and blood specification represses cardiac specification and delimits the capacity of the heart field. This regulatory relationship between cardiovascular pathways suggests new strategies for directing progenitor cell differentiation to facilitate cardiac regeneration.

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Program/Abstract # 17
Cellular and molecular mechanisms controlling lymphatic vasculature development in mammals
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The lymphatic system transports tissue fluid, extravasated plasma proteins, and cells back into the blood circulation. It also contributes to the body's immune surveillance and absorbs lipids from the intestinal tract. Lymphangiogenesis